The effect of pressure- and volume-controlled one -lung ventilation on lung dynamics and plasma malondialdehyde level

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Abstract

Aim: The main purpose of the study was to assess the effects of modes of volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) during one-lung ventilation (OLV) on serum malondialdehyde (MDA), which is the end product of lipid peroxidation. Arterial blood gases, respiratory dynamics, and hemodynamic values were also comparatively investigated. Material and Method: This study is a single-center, prospective, randomized, controlled clinical study was conducted in the Single-center, Thoracic Surgery Operating Room of University Faculty of Medicine. Patients were randomly divided into two groups: Group P (pressure controlled, 20 cases) and Group V (volume-controlled, 20 cases). Following induction, a double-lumen endotracheal tube was placed. Hemodynamics and respiratory parameters were recorded during the operation. For MDA measurements, arterial blood specimens were taken just before the operation (preoperative), after OLV, and 6 hours after the operation. Results: The values of hemodynamics were similar in both groups. Serum MDA measurements were found similar in both groups at preoperative, end of OLV and 6 hours after the operation. Discussion: During OLV the effects of PCV and VCV on plasma MDA levels are not different from each other. Therefore we are of the opinion that selection of PCV or VCV as respiratory mode created no significant differences in oxidative stress.

Introduction

Volume-controlled ventilation (VCV) is the most commonly used mode of invasive mechanical ventilation in one-lung ventilation (OLV) [12]. The application of VCV increases airway pressure. The increased airway pressure in the ventilated lung leads to increased hypoxemia by diverting blood flow to the nonventilated lung and increasing the pulmonary shunt. For this reason, the search for new ventilation strategies in OLV and thoracic surgery is ongoing [3-6].

Acute respiratory distress syndrome (ARDS) and OLV present a similar pathophysiology of hypoxemia; in both situations, hypoxemia is caused by atelectasis, as well as by shunt formation following ventilation/perfusion imbalance [7]. Both in acute lung injury (ALI) and ARDS, the mode of pressure-controlled ventilation (PCV) is used as a protective ventilatory strategy, which prevents the uncontrolled pressure increase in the alveoli [8]. Because of decreased inspiratory flow rate with PCV mode, the peak airway pressure is decreased and PaO_2 is increased [3,9,10]. Regarding this fact, PCV mode is considered to be an alternative ventilation mode to avoid high pressure in the airway [7].

During OLV one lung is fully atelectatic. Hypoperfusion occurs in the nonventilated lung because of hypoxic pulmonary vasoconstriction. Also, the remaining lung tissue after resection is seriously manipulated. With the removal of the bronchial blocker and the following lung reexpansion, large quantities of oxygen radicals are formed [11,12]. The formation of free oxygen radicals is followed by nonenzymatic lipid peroxidation, which is a very toxic chain reaction. Lipid peroxidation directly impairs the cell membrane, and by producing reactive aldehydes, indirectly impairs the other cell components, thus causing tissue damage and various diseases [13-15]. Malondialdehyde (MDA), the primary end-product of lipid peroxidation, is used to detect and quantify lipid peroxidation. Malondialdehyde easily diffuses from its production site. Cross-binding to membrane lipids and proteins changes the original structure of the cell membrane, increasing membrane permeability [13,14].

The main purpose of this study was to assess the effect of VCV and PCV modes on oxidative stress during OLV by measuring serum MDA levels. The other purpose of the study was to assess the effect of different ventilation strategies on respiratory function by measuring lung dynamics and arterial blood gases, and also the effect on hemodynamics.

Material and Method

The prospective, randomised, controlled clinical study was conducted in the Thoracic Surgery Operating Room of University Faculty of Medicine, after obtaining approval from the institutional ethics committee. The patients were informed about the study and written consent was obtained from each patient. Forty patients were included in the study. Age, gender, weight, and smoking history of the patients were recorded.

Inclusion Criteria: 1. Patients with voluntary consent
2. ASA I-II-III patients
3. Hemodynamically stable patients

Exclusion Criteria: 1. Intraoperative massive hemorrhage
2. Impossibility of performing intraoperative OLV

3. Intraoperative malposition of double-lumen endotracheal tube

4. Patients with oxygen saturation below 90% despite the increased FiO_2 during OLV

After the patients were taken to the operating room, electrocardiogram (ECG) and oxygen saturation (SpO_2) were monitored first, and then a 20 G cannula was inserted on the back of the hand to maintain peripheral intravenous access, and 0.03 mg/kg IV midazolam was given for premedication. Under local anesthesia, arterial cannula was placed and arterial blood pressures were monitored. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), SpO_2 values were recorded. As the parameters of mechanical ventilation, tidal volume (TV), respiratory rate (frequency), the mean minute volume (MV), peak pressure, plateau pressure values were recorded throughout the operation. Operation, anesthesia, OLV and double-lung ventilation time periods were also recorded.

Arterial blood samples and blood samples for measurement of malondialdehyde (MDA) were obtained just at the beginning of operation (preoperative), at the end of OLV, and 6 hours after operation.

For the induction of anesthesia, bolus doses of 3-4 µg kg^{-1} fentanyl, 5-7 mg kg^{-1} thiopental, 0.1 mg kg^{-1} vecuronium were given. Anesthesia was maintained with fentanyl, vecuronium, sevoflurane 1 MAC (minimum alveolar concentration), dry air and oxygen mixture. After anesthesia induction, endobronchial intubation was performed by using a double-lumen tube (Broncho-Cath, Mallinckrodt Medical, Athlone, Ireland) and the position of the tube was confirmed by auscultation. Endobronchial tube position was confirmed and adjusted with fiberoptic bronchoscopy. The patients were randomly assigned to pressure-controlled (Group P) and volume-controlled (Group V) and ventilation protocol was applied in these two groups.

For both groups, the PEEP was set to a fixed value of 5 cmH_2O and peak airway pressure (Ppk) was limited to 35 cmH_2O. A dry air-oxygen mixture was used maintaining FiO_2 of 50%. Respiratory rate of 12 breaths/minute during TLV, and 20 breaths / minute during OLV was applied and adjusted to maintain $PaCO_2$ in the 35-45 mm Hg range. When SpO_2 was detected below 90% during OLV, FiO_2 was gradually increased to 60%, 80%, and up to 100 %. For Group V, ventilation was applied with a tidal volume (TV) of 7-8 mL kg^{-1}, and a TV of 4-5 mL kg^{-1} during OLV. Group P ventilation was performed with inspiratory pressure to provide a TV of 7-8 mL kg^{-1} and TV of 4-5 mL kg^{-1}.

To assess the level of MDA, blood samples were taken from the arterial catheter to biochemistry tubes before induction, at the end of OLV, and 6 hours after the operation. The serum samples were stored at -80°C until measurement. MDA levels of the samples were measured by using OxiSelect MDA adduct ELISA Kit (Cell Biolabs, Inc. San Diego, CA 92126, USA) with ELISA method. The minimum MDA level that the kit could detect was 2 pmol mg $^{-1}$ MDA.

The study data were statistically analyzed by using SPSS version 18. Descriptive statistics such as the frequency distribution, mean and standard deviation were used to describe the sample. In the comparison of continuous variables according to the pressure- and volume-controlled groups, testing for the dif-

ference between two medians or the Mann-Whitney U test was used. Comparison of continuous variables within each group was carried out by the two paired test or Wilcoxon test. Correlations of continuous variables within each group were tested by Pearson or Spearman's correlation tests. Chi-square test was used to compare categorical variables according to the groups. To determine statistically significant differences in the analysis, a 95 % level of significance (or α = 0.05 margin of error) was used.

Results

Group P consisted of 20 patients (mean age 49.6 ± 17.4) who underwent pressure-controlled ventilation and Group V consisted of 20 patients (mean age 57.8 ± 13.8) who underwent volume-controlled ventilation. No statistically significant difference was found between the groups in terms of age, weight, height, and gender distribution (P > 0.05) (Table 1).The surgical procedures applied to patients are shown in Table 2.

Three patients, who did not meet the inclusion criteria, were excluded from the study. Two patients in the VCV group were excluded from intraoperative malposition of double-lumen endotracheal tube. Also, one patient in the PCV group did not tolerate OLV and excluded.

When the MDA levels before anesthesia were compared, no significant difference was found between Group P and Group V ($109.9 ± 35.0$ pmol mg^{-1} and $97.1 ± 17.4$ pmol mg^{-1}, P : 0.20), At the end of OLV, MDA levels were not significantly different in the groups (respectively, $107.5 ± 33.8$ pmol mg^{-1}and $112.4 ± 40.0$ pmol mg^{-1}, P = 0.80). Six hours after the end of the operation, MDA levels again showed no significant difference between the groups (respectively, $116.3 ± 45.9$ pmol mg^{-1} and $119.8 ± 50.9$ pmol mg^{-1}, P = 0.70) (Table 3).

In both groups, the heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and mean arterial pressure (MAP) showed similar course during the operation. FiO_2 and SpO_2 values showed no significant difference between the groups (P > 0.05) (Table 4). VT was found to be lower in the PCV group than the VCV group after intubation, 15 and 45 minutes after the initiation of OLV, and at the end of OLV (P < 0.05) (Table 5). The peak pressures were also evaluated, and found to be lower in the P group than the group V 15, 30 and 45 minutes after the initiation of OLV (P < 0.05) (Table 5). The values of plateau pressure and respiratory minute volume were similar in both groups.

No statistically significant difference was detected between the PCV and VCV groups in terms of pH, PaO_2, $PaCO_2$, hematocrit, hemoglobin, sodium, potassium, calcium, bicarbonate and lactate values (P > 0.05). PaO_2 and $PaCO_2$ values were presented in Table 6.

Discussion

In one lung ventilation, the two most important features for anesthetist are prevention of hypoxia and prevention of acute lung injury which causes significant morbidity and mortality [16]. With the development in anesthetic drugs and equipment, hypoxia can be prevented easily. In our study, PaO_2 levels were similar in both groups. Attention is directed to the prevention of acute lung injury. In our study, in VCV treatment group 7-8 mL

kg^{-1} TV with 5 cmH$_2$O PEEP was applied. Traditionally, 10-12 mL kg^{-1} TV implementation was proposed, but this level of TV leads to stress in the lung parenchyma and alveoli, and causes acute lung injury [16,17]. From the other direction, less than 8 mL kg^{-1} TV has a risk of development of atelectasis. For these reasons, in our study 7-8 mL kg^{-1} with 5 cmH$_2$O was applied and both atelectasis and volume of trauma are prevented.

With the PCV application optimal peak airway pressure prevents barotraumas to lung parenchyma (8). The same time, it prevents hypoxia via preventing shunt from dependent lung to independent lung. In our study, TV and Ppeak levels were lower in PCV group than VCV group. PaO_2 levels were similar in both groups. These findings suggest that PCV mode provides adequate oxygenation with lover Ppeak and TV levels.

Various studies were compared the PCV and VCV modes (3,10,19). Tugrul et al. [3] have reported that PCV improves oxy-

Table 1. Distribution of the age, weight, height and gender of the cases

	GROUP P N = 20 Mean ± Standard Deviation	GROUP V N = 20 Mean ± Standard Deviation
Age (year)	49.6 ± 17.4	57.8 ± 13.8
Weight (kg)	71.3 ± 12.3	74.8 ± 13.6
Height (cm)	168.6 ± 6.1	168.7 ± 5.1
Gender (male/ female)	11/9	14/6
OLV duration (min)	46.2 ± 27.2	56.17 ± 33.1
COPD (n)	7	8
Smoking history (n)	8	11

Group P: pressure controlled ventilasyon group, Group V: volume controlled ventilasyon group, OLV: One-lung ventilation, COPD: chronic obstructive pulmonary disease, Inter groups comparisons * means statistically significant (P <0.05)

Table 2. Distribution of the Operations Between Group P and Group V

	Group P N = 20	Group V N = 20
Right Upper Lobectomy	3	3
Pulmonary Biopsy	3	2
Right Lower Lobectomy	3	2
Sympathectomy	2	2
Wedge Resection	2	2
Right Pneumonectomy		2
Excision of Pulmonary Nodule	1	
Left Lower Lobectomy		1
Resection of Pulmonary Bullae	2	1
Removal of Pulmonary Tumor	4	5

Group P:pressure controlled ventilasyon group, Group V:volume controlled ventilasyon group

Table 3. Comparison of MDA Concentrations Between Group P and Group V

MEASURED MDA VALUES (pmol/mg)	Group P N = 20 Mean± Standard Deviation	Group V N = 20 Mean ± Standard Deviation	P values
MDA Preoperative	109.9 ± 35.0	97.1 ± 17.4	P : 0.20
MDA End of OLV	107.5 ± 33.8	112.4 ± 40.0	P = 0.80
MDA 6h after operation	116.3 ± 45.9	119.8 ± 50.9	P = 0.70

Group P: pressure controlled ventilasyon group, Group V: volume controlled ventilasyon group MDA: malondialdehyde, OLV: One-lung ventilation, Inter groups comparisons * means statistically significant (P < 0.05)

genation during OLV compared with VCV. In contrast Unzueta et al. [19] suggested that PCV for OLV did not lead to improved oxygenation compared VCV. In our study, like in the study of Unzueta et al., there was no difference in the oxygenation level between the VCV and PCV groups. Our findings suggested that, in VCV group, lung protective strategies with low TV with PEEP application achieve adequate oxygenation. Decrement of Ppeak and TV seems to be a partly advantage in PCV application.

The use of OLV in lung surgery is a cause of serious oxidative stress [20, 21]. The oxidative stress is normally balanced *by the endogenous antioxidant* system [22, 23]. If oxidative stress generated by an excess of free oxygen molecules cannot be balanced by the antioxidant system, they gradually accumulate. The free oxygen radicals which are highly reactive chemically because of their unpaired electrons interact with the structural molecules of cells, impairing mostly the function of endothelial cells [23]. During application of OLV, many factors contribute to the induction of oxidative stress; the damage in the ventilated lung, as well as the reexpansion and reperfusion in the nonventilated lung are factors that play a role in inducing oxidative stress. The high concentration of oxygen present in the ventilated lung during OLV is one of the sources of oxidative stress; the intraoperative manipulation of the nonventilated lung tissue during OLV is another source [20]. During OLV, the atelectasis and consequent hypoxic pulmonary vasoconstriction in the ventilated lung cause hypoxic injury [20, 23]. The reperfusion of hypoxic tissues paradoxically causes further cellular damage. The application of high inspired oxygen concentrations to and reexpansion of the contralateral lung causes reactive pulmonary vasodilatation and sudden reoxygenation of ischemic cells ensued by oxidative stress [23]. The oxidative stress induced by reexpansion and reperfusion is associated with early postoperative oxidative stress [20].

In both groups, all through the duration of OLV hypoxia was prevented by increasing FiO_2 values. During OLV, there was no significant difference in FiO_2 values between the two groups (Table 4). Lipid peroxidation is the most important metabolic result of oxidative stress [14, 15]. This study on the levels of MDA, which is a marker of oxidative stress, showed that during OLV the effects of PCV and VCV on plasma MDA levels are not different from each other. These findings indicate that neither PCV mode nor VCV mode affects the total oxidative stress level. At this stage, the selected ventilation mode has no effect on the control of oxidative stress sources, namely, excessive oxygenation of the ventilated lung, surgical trauma, and manipulation of lung tissue. For this reason, we think that the ventilation mode selected in OLV would play no major role in avoiding oxidative stress.

In both groups, the serum MDA levels were still high 6 hours after the end of OLV. At this stage, the main source of oxidative stress is reexpansion and reperfusion. Also at this stage, the selection of PCV or VCV as respiratory mode created no significant differences in serum MDA levels.

It is concluded that lung protective strategies with low TV with PEEP application achieve adequate oxygenation. The decrement of Ppeak and TV seems to be a partly advantage in PCV application. Various mechanisms are responsible for oxidative stress in OLV and using of the ventilation mode would have no effect on these mechanisms. During OLV, the effects of PCV and VCV on plasma MDA levels are not different from each other. Therefore, we are of the opinion that selection of PCV or VCV as respiratory mode created no significant differences in oxidative stress.

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